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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/628,905	07/28/2003	Gregory F. Brooks	17310CIP1CON1 (BOT)	7440

7590 09/17/2004

STEPHEN DONOVAN
ALLEGAN, INC.
T2-7H
2525 Dupont Drive
Irvine, CA 92612

EXAMINER	
TONGUE, LAKIA J	

ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 09/17/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/628,905	BROOKS ET AL.	
	Examiner	Art Unit	
	Lakia J Tongue	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 July 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *19,20 and 22-24* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *19,20 and 22-24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *7/28/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's response filed on July 13, 2004. Claims 19 and 22 have been amended. Claim 21 is canceled. Claims 19, 20 and 22-24 are under examination.

The text of those sections of Title 35, U.S. Code not included in this action can be found in the prior Office Action.

Objections Withdrawn

1. In view of Applicant's amendment and response, the following objections are withdrawn:

a) objection to the specification, page 2, paragraph 1 and 3.

Rejections Withdrawn

2. In view of Applicant's amendment and response, the following rejections are withdrawn:

a) rejection to claim 21 under 35 U.S.C. 112, second paragraph, page 3, paragraph 6 and 7.

b) rejection to claims 19 and 20 under 35 U.S.C. 101, page 3, paragraph 8 and 9.

c) rejection to claims 19-23 under 35 U.S.C. 102(b), page 4, paragraph 13.

d) rejection to claims 19-24 under 35 U.S.C. 102(b) and (e), page 6, paragraph 14.

Objections Maintained

3. The objection to the specification under 37 CFR 1.58, MPEP 608.01 as having no page numbers is maintained for the reasons set forth on page 2, paragraph 4.

New Grounds of Objection/Rejection

Specification

4. The specification is objected to as failing to provide proper antecedent basis for the claimed subject matter. See 37 CFR 1.75(d)(1) and MPEP § 608.01(o). The specification as filed fails to provide antecedent basis for the recited function of "wherein the botulinium toxin elutes from the stent". Applicants are specifically cautioned against adding material from the parent applications in view of the issues regarding the recitation of "incorporation by reference" set forth below.

The amendment filed July 28, 2003 is objected to under 35 U.S.C. 132 because it introduces new matter into the disclosure. 35 U.S.C. 132 states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows: the oath/ declaration, transmittal letter and the original specification

introduce new matter because they conflict with regard to the particular relationships of the parent with the instant application. The preliminary amendment filed 7-28-03 states that the instant application is a continuation of USSN 10/114,740 and the transmittal cover letter states that the instant application is a continuation-in-part of USSN 10/114,740. The oath and declaration provides no clarification of this issue. Further, the marked up version of the preliminary amendment recites paragraphs at page 6 and 7, that are not in fact present in the specification as filed (see attached pages). A continuation is an ipsis verbis or nearly identical disclosure. The marked up copy provides for a disclosure at pages 6 and 7 that is substantially different in nature. In view of the conflict as recited above, the insertion of the term "continuation of" by the preliminary amendment is considered new matter. Further, the marked up copy is in conflict with the clean copy because the clean copy does not recite the phrase "The entire contents of these prior patent applications are incorporated herein by reference." Therefore, the preliminary amendment filed 7-28-03 was clearly not in compliance with any amendment practice at the time that the invention was filed.

With regard to the attempt to incorporate the prior applications by reference in the underlined amendment, the statement that the prior application is "incorporated by reference" is in fact also new matter.

United States Patent and Trademark Office OG Notices: 18 March 2003 Claiming the Benefit of a Prior-Filed Application under 35 U.S.C. 119(e), 120, 121, and 365(c) Part VII: Adding an Incorporation-By-Reference Statement in a

Benefit Claim is Not Permitted After Filing An incorporation-by-reference statement added after the filing date of an application is not permitted because no new matter can be added to an application after its filing date. See 35 U.S.C. 132(a). If an incorporation-by-reference statement is included in an amendment to the specification to add a benefit claim after the filing date of the application, the amendment would not be proper. When a benefit claim is submitted after the filing of an application, the reference to the prior application cannot include an incorporation-by-reference statement of the prior application. See Dart Industries v. Banner, 636 F.2d 684, 207 USPQ 273 (C.A.D.C. 1980). Therefore, the Office will not grant a petition to accept a benefit claim that includes an incorporation-by-reference statement of a prior application, unless the incorporation-by-reference statement was submitted on filing of the application.

Even if the amendment was in compliance with any of the amendment rules or provisional amendment practice pursuant to 37 CFR 1.121 on July 28, 2003, it still would have been new matter because any preliminary amendment attempting to recite the "incorporation by reference" that was not specifically referenced in the oath or declaration or the transmittal papers is NOT considered part of the filing of the application (see cited section of the appropriate OG notice above).

Double Patenting

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an

invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

5. Claim 23 of this application is rejected under 35 U.S.C. 101 as claiming the same invention as that of claim 13 and 14 of prior U.S. Patent No. 6,767,544 B2. This is a double patenting rejection.

The claims in the instant application are drawn to a stent comprising a botulinum toxin attached or embedded therein. The claims of the patent are drawn to a composition comprising the sole element as a stent with a botulinum neurotoxin attached or embedded therein. The recitation of "neurotoxin" as opposed to "toxin" does not define a structural difference between the claimed toxins because the terminology of botulinum toxin and botulinum neurotoxin is used interchangeably in the specification and in the art. Should applicant wish to dispute the interpretation of this language in view of the specification, they should specifically point to the specification that clearly and unambiguously teaches the differences between "toxin" and "neurotoxin".

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686

F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

6. Claims 19, 20, 22 and 23 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 13 and 14 of U.S. Patent No. 6,767,544 B2 in view of Donovan et al US Patent 6,383,509.

As to claims 19, 20 and 22, the claims in the instant application are drawn to a stent comprising a botulinum toxin attached or embedded therein wherein the botulinum toxin elutes from the stent and dependent claims reciting toxin types A-G.

The claims of the '544 patent are drawn to a composition comprising as the sole element a stent with a botulinum neurotoxin attached or embedded therein and dependent claims reciting neurotoxin type A (claims 13 and 14). The scope of the term "botulinum toxin" and "botulinum neurotoxin" is unclear because it appears that the specification uses the terms interchangeably for example the specification teaches: "The anaerobic, Gram positive bacterium *Clostridium botulinum* produces a potent polypeptide neurotoxin, botulinum toxin, which causes a neuroparaltic illness in humans and animal referred to as botulism."

Donovan et al '509 teaches a composition comprising a matrix to which botulinum toxin is attached or imbedded (columns 23, lines 39-40) and takes the shape of a rod or tube (i.e. the instant stent; column 17, lines 35-40) or is incorporated into a matrix of a carrier polymer (column 24, lines 1-13) and the matrix with the botulinum toxin attached or imbedded therein is inserted in a type of tubular structure for injection or implantation (column 13, lines 52-56). The matrix provides for the advantage of a continuous or controlled release (see column 17, lines 3-10) that provides a therapeutically effective amount with negligible serum levels (see column 17, lines 16-23).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time that the invention was made to modify the stent of the '544 patent by incorporating the toxin into a carrier matrix that elutes from the matrix for continuous or controlled release as a means for providing the advantages of delivering a therapeutically effective amount over an extended period of time with negligible serum levels as taught by Donovan et al '509 to arrive at the instantly claimed invention of having the toxin elute from the stent.

As to claim 23, the instant claim recites a stent comprising a botulinum toxin attached or embedded therein. The scope of the term "toxin" as opposed to "neurotoxin" is not defined by the specification. In the event that the specification provides a different structure and function for neurotoxins as opposed to toxins per se, claim 23 as drawn to the genus toxins is anticipated by the patented subgenus "neurotoxin" recited in the claims of the '544 patent and specifically recited toxin A.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 19, 20 and 22 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Claims 19, 20 and 22 now recite that the toxin elutes from the stent. This specification fails to describe any matrix or material or the function of eluting from any stent. The amendment of 7-28-03 indicates that support may be found in the parent Application 09,371,354. Applicants cannot rely upon a parent application for subject material not disclosed nor taught in the instant specification because attempt to rely upon the preliminary amendment to "incorporate the teachings of the parents by reference" and in particular 09,371,354 is improper and introduces new matter. Consequently, the term is new matter to the claims. This issue is best resolved by Applicants pointing to the instant specification by page and line number where written description support for this concept can be found.

For purposes of the art rejections set forth for claims 19, 20 and 22 below, it is noted that Applicants are not entitled to the earlier filing date because both

the instant application and parent 10/114,740 fails to provide conception by way of written description for the recitation of "wherein the botulinum toxin elutes from the stent". It is further noted that Applicant(s) cannot rely upon parent 09/371,354 for support for the language because the "incorporation by reference" was deemed new matter as set forth supra. As such, the filing date for prior art purposes is the instant filing date of 7-28-03.

For purposes of the art rejections set forth for claims 23 and 24 are not supported by application 09/371,354 because the specification was not enabled for how to use such as evidenced by the rejections under 112 1st ¶ set forth therein. As such the filing date for prior art purposes for these claims has been assigned the date 4/1/02.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

8. Claims 19, 20, and 22 are rejected under 35 U.S.C. 102(b) as being anticipated by Donovan et al, U.S. Patent 6,383,509 B1.

Claims 19, 20 and 22 are drawn to a composition comprising a stent with a botulinum toxin attached or embedded wherein the botulinum toxin elutes from the stent.

(Stedman's Medical dictionary: stent: 1. A thread, rod, or catheter, lying within the lumen of tubular structures, used to provide support during or after their anastomosis, or to assure patency of an intact but contracted lumen)

Donovan et al, U.S. Patent 6,383,509 B1 discloses a composition that comprises a stent to which botulinum toxin is attached or imbedded (column 24, lines 2-6), wherein the botulinum toxin may be all of the botulinum serotypes A, B, C, D, E, F and G (column 23, lines 39-40), any one of the serotypes (column 12, line 43-46; column 11, lines 21-24).

The composition is formulated for injection or implantation (column 11, line 60) and takes the shape of a pellet, disc, rod, tube, film, microsphere (column 17, lines 35-40 and column 22, lines 12-30) or is incorporated into a matrix of a carrier polymer (column 24, lines 1-13). The matrix with the botulinum toxin attached or embedded therein, is inserted into a type of tubular structure for injection or implantation (column 13, lines 52-56).

One look dictionary search defined elution as the process of extracting one material from another by washing with a solvent to remove adsorbed material from an adsorbent. The concept of elution of continuous release (column 17, lines 26 and 31) is in fact an elution from the stent.

The reference anticipates the instantly claimed invention.

Claims 23 and 24 are rejected under 35 U.S.C 102(b) as being anticipated by Murkerjee et al, (Expandable Metal Stents in Achalasia- Is There a Role?, November 9, 2000, Elsevier Science Inc., Vol. 95, 2185-2187).

The claims are drawn to a composition comprising a stent with a botulinum toxin embedded or attached. The claims are also drawn to a stent with botulinum toxin types attached or embedded.

Murkerjee et al. teach a composition comprising a stent and botulinum toxin (see table 1, page 2186). The composition and stent of Murkerjee et al. is the same as the claimed composition. Characteristics such as embedded or attached toxin elutes from the stent are being viewed as process limitations. Additionally the recitation of "for use in" is being viewed as an intended use recitation, which does not impart patentability to the product.

Claims 23 and 24 are rejected under 35 U.S.C. 102(e) as being anticipated by Unger U.S. Patent 6,579,847. In light of the enablement issues set forth above, claims 23 and 24 are considered to have a filing date of 4/1/02.

The claims are drawn to a stent and an angioplasty balloon comprising the botulinum toxin attached or embedded therein.

Unger teaches an angioplasty balloon and a stent with botulinum toxin A attached. The stent and angioplasty balloon are the same as the claimed composition comprising a stent with botulinum toxin attached and the angioplasty balloon with botulinum toxin attached (columns 3-6). Characteristics such as botulinum toxin elutes from the stent are being viewed as process limitations

which do not impart patentability to the product. Additionally, the recitation of "for use" is being viewed as intended use.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. Claims 19, 20, 22, 23 and 24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Vigil et al, U.S. Patent 6,102,904 in view of Schramm et al, U.S. Patent 6,121,296 and Rappuoli et al (Guidebook to Protein Toxins and Their Use in Cell Biology, 1997, Oxford University Press, pages 66 and 108.).

The claimed invention is directed to a composition that comprises a stent with a botulinum toxin attached or embedded wherein the botulinum toxin elutes from the stent or an angioplasty balloon comprising a botulinum toxin attached or embedded therein.

Vigil et al. discloses a device for injecting into a wall of a blood vessel. Vigil et al teaches a composition for use in a cardiovascular procedure (see figures). Figures 9-11 depict an inflatable balloon with multiple dispensing ports (little cups) within. The figure would meet the limitation of imbedded therein. If the toxin were in the dispensing ports the toxin would clearly be embedded therein.

Vigil et al teaches a composition for use in a cardiovascular procedure (see figures) comprising a stent (see abstract) with a toxin attached or embedded therein (column 3, lines 33-46), wherein the composition comprises a device with a multi-lumen catheter in which a toxin containing fluid resides for the injection of a blood vessel to treat stenosis. Vigil et al teaches administration of a toxin directly to a blood vessel (column 1, lines 23-30) of a patient, wherein the composition is administered during or after a cardiovascular procedure comprising a composition comprising a tube or balloon (column 4, lines 16-24) with a toxin attached or imbedded in dispensers therein (column 11, lines 47-54; column 3, lines 33-46) and the administering is accomplished through injection of a toxin containing fluid into the vessel. The injection device comprises an expandable multi-lumen catheter that administers the toxin containing fluid or slow release composition directly into a blood vessel. However, Vigil et al teaches suitable toxins such as pseudomonas exotoxin or Ricin A toxin (column 3, line 44). Vigil et al differs because they do not teach the limitation of a botulinum toxin.

Schramm et al has priority back to November 4, 1992. Application number 08/781,745 (page 3, lines 8-15) also teaches that pseudomonas toxins and botulinum toxins are both ADP-ribosylation toxins. ADP-ribosylation toxins are common in bacterial infections. These toxins include but are not limited to pseudomonas enterotoxin and botulinum toxin (column 3, lines 4-9).

Rappuoli et al (1997) teaches that when you combine botulinum neurotoxin type C strains with D strains they will produce the Clostridium

botulinum C2 toxins and the botulinum C3 ADP-ribosyltransferase (page 108, 2nd ¶). Rappuoli also teaches the C2 toxin to be an ADP-ribosyltransferase (page 66, 2nd column).

It would have been *prima facia* obvious to a person having ordinary skill in the art at the time the invention was made to modify the composition of Vigil et al that comprises a expandable stent or balloon and a toxin to substitute the botulinum toxin of Rappuoli et al because Schramm et al teach both pseudomonas toxin and botulinum toxin function as ADP-ribosylating toxins, and substitution of one functional equivalent for another is routine in the art.

Since the Office does not have the facilities for examining and comparing applicants' composition with the composition of the prior art, the burden is on applicant to show a novel or unobvious difference between the claimed product and the prior art (i.e., the composition of the prior art does not posses: a stent with botulinum toxin attached). See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

Conclusion

10. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Muniyappa, R. et al., Am. J. Physiol. Heart Cir. Physiol., vol. 278, (6) pages H1762-H1768, June 2000. Muniyappa et al teach botulinum toxins C3 and B as inhibitors of Rho, which increases iNOS expression in an analogous art for the purpose of showing (23 and B botulinum toxins as

therapeutic agents for the prevention of restenosis associated with vascular injury (see page H1767).

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lakia J Tongue whose telephone number is 571-272-2921. The examiner can normally be reached on Monday-Friday 7-3:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on 571-272-0864. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Ljt

Patricia A. Duffy
PATRICIA A. DUFFY
PRIMARY EXAMINER